



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁵ : C08B 37/08	A1	(11) International Publication Number: WO 91/00298 (43) International Publication Date: 10 January 1991 (10.01.91)
(21) International Application Number: PCT/FI90/00173 (22) International Filing Date: 2 July 1990 (02.07.90) (30) Priority data: 893223 30 June 1989 (30.06.89) FI (71) Applicants: FIREXTRA OY [FI/FI]; Yliopistonkatu 45 D 36, SF-33500 Tampere (FI). INSTYTUT WŁÓKIEN CHEMICZNYCH [PL/PL]; ul. M.C. Skłodowskiej 19, 90-570 Łódź (PL). (72) Inventors: STRUSZCZYK, Henryk ; ul. Tuwima 8/29, 95-100 Zgierz (PL). NIEKRASZEWICZ, Antoni ; ul. 11 Listopada 41/9, Lodz (PL). WRZEŚNIEWSKA-TOSIK, Krzystyna ; ul. P. Skargi 87, 95-200 Pabianice (PL). KOCH, Stanisław ; ul. Biernackiego 8-10/29, Tomaszów Mar. (PL). KIVEKÄS, Olli ; Näsälinnankatu 12 A 3, SF-33210 Tampere (FI).		(74) Agent: HAKOLA, Unto; Tampereen Patenttitoimisto Oy, Kanslerinkatu 6, SF-33720 Tampere (FI). (81) Designated States: JP, NO, SU. Published <i>With international search report.</i>
(54) Title: METHOD FOR CONTINUOUS MANUFACTURE OF MICROCRYSTALLINE CHITOSAN (57) Abstract <p>In a method for continuous manufacture of microcrystalline chitosan by precipitation of chitosan from its aqueous solutions in organic or inorganic acid, or their salts, the chitosan solution in an aqueous acid solution, especially in acetic acid, with polymer concentration not lower than 0.01 wt%, preferably with polymer concentration within 0.1-2.0 wt%, is continuously introduced into a reactor together with an alkaline solution, such as an aqueous solution of an alkaline metal hydroxide or a salt thereof having a concentration ranging from 0.1 to 20.0 wt%. The chitosan solution is introduced into the reactor with a rate within a range of 0.1-20 volume parts per 1 hour and 1 reactor volume part, and the alkaline solution is introduced into a reactor with a rate ranging from 0.1 to 10.0 volume parts per 1 hour and 1 reactor volume part to obtain a mixture pH of equal to or higher than 7. The microcrystalline chitosan dispersion having said pH is simultaneously taken off from the reactor by a continuous system with a rate suitable to keep a constant reaction mixture volume in the reactor, and the microcrystalline chitosan dispersion is collected in a compensation tank and is continuously purified, especially by continuous water washing or by ultrafiltration method. The purified microcrystalline chitosan is finally concentrated to obtain a polymer content of 0.5-10.0 wt% and dried by some well-known method.</p>		

DESIGNATIONS OF "DE"

Until further notice, any designation of "DE" in any international application whose international filing date is prior to October 3, 1990, shall have effect in the territory of the Federal Republic of Germany with the exception of the territory of the former German Democratic Republic.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria	ES	Spain	MC	Monaco
AU	Australia	FI	Finland	MG	Madagascar
BB	Barbados	FR	France	ML	Mali
BE	Belgium	GA	Gabon	MR	Mauritania
BF	Burkina Faso	GB	United Kingdom	MW	Malawi
BG	Bulgaria	GR	Greece	NL	Netherlands
BJ	Benin	HU	Hungary	NO	Norway
BR	Brazil	IT	Italy	RO	Romania
CA	Canada	JP	Japan	SD	Sudan
CF	Central African Republic	KP	Democratic People's Republic of Korea	SE	Sweden
CG	Congo	KR	Republic of Korea	SN	Senegal
CH	Switzerland	LI	Liechtenstein	SU	Soviet Union
CM	Cameroon	LK	Sri Lanka	TD	Chad
DE	Germany, Federal Republic of	LU	Luxembourg	TC	Togo
DK	Denmark			US	United States of America

Method for continuous manufacture of microcrystalline chitosan

- 5 This invention relates to continuous manufacture of microcrystalline chitosan. Up to now there is known a method for manufacture of chitosan by a periodical system, the chitosan so manufactured having developed intrinsic surface. The method is based on periodical
10 precipitation of chitosan with especially a deacetylation degree higher than 30%. The chitosan is dissolved in the aqueous solution of organic or inorganic acid, and it is precipitated by aqueous solutions of alkaline metal hydroxides with application of strong stirring.
15 The precipitated chitosan in a form of gel or dispersion is subjected to a purification process by several water washing. There is also known a method of manufacture of precipitated chitosan in a form of gel or dispersion preceded by a thermal degradation process
20 realized by organic or inorganic acid treatments in a temperature not lower than 50°C and in a time not shorter than 1 hour. The well-known methods permit to obtain chitosan with a yield ranging within 70-90%. The well-known methods are carried out in the reactors
25 having stirrers or having homogenizers. The well-known methods are described in the Polish Patent of 125 995 as well as in "Journal of Applied Polymer Science", vol. 33, page 177, 1987.
- 30 Periodical system of manufacture of microcrystalline chitosan causes that its production cycle is time-consuming, taking up time not less than 12-24 hours. It also causes high consumption of energy as well as washing water. The microcrystalline chitosan obtained
35 is characterized by heterogeneous properties in the respective portions. The well-known method does not allow to obtain microcrystalline chitosan with homogeneous properties.

The object of this invention is continuous manufacture of microcrystalline chitosan, by continuous precipitation of microcrystalline chitosan by an aqueous solution of alkaline metal hydroxides from the standard chitosan dissolved in an aqueous organic or inorganic acid, or in a solution of their salts.

In accordance with a preferred embodiment of a method of the invention, the continuous manufacture of microcrystalline chitosan by initiation of chitosan precipitation from its aqueous solution in the organic or inorganic acids or their salts, by an aqueous solution of alkaline metal hydroxides or their salts, comprises that a chitosan solution in the an aqueous acid solution, especially acetic acid with polymer concentration not lower than 0.01 wt%, is introduced by a continuous system to a reactor, together with an aqueous solution of an alkaline metal hydroxides or a salt thereof, especially with an aqueous sodium hydroxide solution with a concentration of 0.1-20 wt%. At the same time the chitosan solution is introduced into a reactor with a rate of 0.1-20 volume parts per 1 hour and per 1 volume part of working reactor capacity, whereas the alkaline solution is introduced with a rate of 0.1-10 volume parts per 1 hour and per 1 volume part of working reactor capacity. The reagent introduced into a reactor with the above rate assures the maintenance of the pH of the reaction mixture on a level equal to or higher than 7. At the same time from a reactor microcrystalline chitosan dispersion with a pH equal to or higher than 7 is withdrawn by the continuous system with a rate necessary to maintain a constant volume of the reaction mixture. Next the microcrystalline chitosan dispersion is stored into a container and then it is purified by the continuous water washing or by the ultrafiltration technique, the purification being continued to a moment where the

conductivity of the effluent is equal to the conductivity of the water used. Purified microcrystalline chitosan dispersion is subjected to eventual concentration to the polymer content of 0.5-10.0 wt% and drying by the well-known methods.

According to a preferred embodiment of the invention, the continuous manufacture of microcrystalline chitosan comprises also that a chitosan solution in aqueous solutions of acids, and the aqueous solutions of alkaline metal hydroxides as well as their salts are introduced continuously with a rate described above into a reactor equipped with a system of continuous circulation and the product is circulated in a closed reactor system, and at the same time a stream of microcrystalline chitosan is continuously withdrawn. The stream is divided in two parts. The first part is returned into the reactor and the second part is directed to a compensation tank and then it is purified. The microcrystalline chitosan dispersion is taken off from the reactor with a rate suitable to keep a constant volume of reaction mixture in the reactor. The application of an additional circulation allows to obtain microcrystalline chitosan with a high degree of properties of homogeneity. In the aim of further enlargement of the degree of homogeneity of the content as well as improvement of the properties of microcrystalline chitosan, an aqueous solution of alkaline metal hydroxide is introduced directly into the circulation system of the reactor.

The method according to the invention allows to obtain a microcrystalline chitosan in a form of dispersion characterized by properties suitable for colloids and distinguished by the water retention value of WRV up to 5000%, particles dimension ranging from 0.1 to 50µm as well as dispersion form stability. A dried product is characterized by a powder form with a particles

dimension within 1-100 μ m and it is distinguished by WRV of 200-600%, crystallinity index KrI up to 95% and a minimal dispersion of chitosan parameters. The method according to the invention allows to obtain a high yield of products on a level of 95-99% in relation to the amount of standard chitosan used, and at the same time the method assures the reduction of raw materials and energy consumption as well as the reduction of manufacturing costs, and also the elimination of arduous operation, in comparison to a periodical process. An important object of method according to the invention is to reduce time for microcrystalline chitosan manufacture in comparison to a periodical method. The investigations have shown that a microcrystalline chitosan obtained according to the method of the invention in a time of 1-5 hours is related to an amount of product produced in a time of 12-24 hours according to a periodical method. Another important object of the method according to the invention is to assure the continuous precipitation of microcrystalline chitosan with required particles dimensions as well as properties, regulated by the concentration, the introduction rate of the reagents and also eventually by dispersion circulation rate in a reactor. A method according to the invention allows to manufacture homogenous products with reproducible parameters in a time of production without outside intervention which has required time in the periodical method.

Microcrystalline chitosan obtained by the method according to the invention is applied to the polymeric films formation in the chemical industry, medicine, pharmaceutical as well as cosmetic industries and also in agriculture.

A method for continuous manufacture of microcrystalline chitosan according to the invention is realized by an

installation, which as an example is presented on the appended schematic figure.

The installation for microcrystalline chitosan manufacture is equipped with a reactor 1 containing a stirrer 2. In the upper part of the reactor vessel there is a pipe 3 for introduction of chitosan solution and a pipe 4 for introduction of the precipitating agent, such as hydroxide solution. A pipe 5 for microcrystalline chitosan dispersion drained off from the reactor 1 is equipped with a pump 6, whose exit is joined to a circulation system 7 for continuous returning of part of dispersion into the reactor 1 and secondly the exit is joined to a pipe 8 for the dispersion conveyed into a compensation tank 9. The pipe 5 is located in a lower part of the reactor 1. The compensation tank 9 is joined to an installation 10 for continuous purification of microcrystalline chitosan dispersion, which is equipped with pipes 11 for introduction and draining of purification water as well as with a pipe 12 for the draining of the purified product. The installation 10 can have also the form of a ultrafiltration system. Additionally, the circulation system 7 of the reactor 1 is equipped in its upper part with a pipe 13 for introduction of the precipitating agent, such as hydroxide solution.

The action of the installation is the following: The initiation of the precipitation process after the raw materials introduction into the reactor 1 with the working stirrer 2 is performed such that the raw materials are continuously introduced into the reactor 1. A hydroxide solution is introduced into the reactor 1 by the pipe 4, or by the pipe 13 into the circulation system 7, in dependence of the chosen system. The neutralization of the reaction mixture up to the value of pH equal to or higher than 7 takes place in the reactor 1 with continuous stirring and

optional dispersion circulation. The microcrystalline chitosan dispersion obtained is simultaneously taken off from the reactor 1 by a continuous system by the pipe 5 and it is completely conveyed into the compensation tank 9, or it is divided in two parts whereof the first is conveyed into the compensation tank 9 and the second part is introduced into the circulation system 7 and returned into back into the reactor 1. The microcrystalline chitosan present in the compensation tank 9 is next delivered into the purification installation 10. The microcrystalline chitosan is delivered after purification to a storage installation or to a dryer.

The invention is explained further in the following examples which do not restrict the scope of claims.

Example 1.

500 volume parts of 1% chitosan solution in a 4% aqueous solution of acetic acid and 2.5% aqueous sodium hydroxide solution are introduced into a reactor of the type presented on the Figure having the working volume of 1000 volume parts. The chitosan used in the reaction was characterized by average molecular weight of 6.07×10^5 , deacetylation degree of 71.8% and WRV of 129%. The dispersion of microcrystalline chitosan was precipitated with the working stirrer to obtain a pH of 8.0 and then, by a continuous system, a 1% chitosan solution in 4% aqueous acid solution with an introduction rate of 2400 volume parts per 1 hour and a 4% aqueous hydroxide solution with an introduction rate of 1728 volume parts per 1 hour were introduced to obtain a mixture pH of 8.0 ± 0.3 . At the same time, microcrystalline chitosan dispersion was taken off from the reactor with a rate suitable to keep a constant volume of mixture in the reactor. Then the dispersion was delivered into a

compensation tank and it was next continuously delivered into a purification installation, where it was continuously washed by water to obtain a product with an EMP value of 28mV (electromotive power),
5 whereas the initial product was characterized by the EMP value of 95 mV. The product was obtained in a form of stable gel with a white colour and it was characterized by a microcrystalline chitosan content of 2.45 wt% calculated on a dry polymer weight, WRV of
10 906% and an average molecular weight of 3.59×10^5 . The product yield was 30.9 weight parts of microcrystalline polymer per 1000 volume parts of reactor and 1 hour.

15

Example 2.

400 volume parts of 1.0% solution of chitosan with
20 the properties shown in Example 1 in a 4% aqueous acetic acid solution were introduced into the reactor as in Example 1. The microcrystalline chitosan dispersion was precipitated under continuous stirring with 2.5% aqueous sodium hydroxide solution to obtain a
25 mixture of pH 7.5, whereas 1.0% chitosan solution in a 4% aqueous acetic acid solution with introduction rate of 2940 volume parts per 1 hour and 2,5% aqueous sodium hydroxide solution with a rate of 3060 volume parts per hour were continuously introduced into the
30 reactor to obtain a mixture reaction having a pH of 7.5 ± 0.2 . The microcrystalline chitosan formation process was realized with the incorporated circulation system characterized by a rate of circulation of 2940 volume parts per 1 hour. At the same time the precipitated microcrystalline chitosan dispersion was
35 taken off for a compensation tank with a rate suitable to keep a constant volume in the reactor. Next the microcrystalline chitosan dispersion with a value of

EMP of 112 mV was delivered to a purification installation to obtain an eluate with an EMP value of 34 mV.

5 The product was obtained in a form of stable gel with a white colour and yield of 30.9 weight parts of microcrystalline chitosan per 1 hour and 1000 volume parts of reactor. The product was characterized by 4.8 wt% of microcrystalline chitosan calculated on a dry weight of polymer, and WRV of 3993%.

10

Example 3.

15 The microcrystalline chitosan dispersion was made in the reactor as in Example 1 with the application of an 1% chitosan solution in a 4% aqueous acetic acid solution with an introduction rate of 3780 volume parts per 1 hour and with the application of 4% aqueous sodium hydroxide solution with the rate of 3960 volume parts per hour, maintaining other conditions as in Example 1.

20

25 The product was obtained in a form of stable gel with a white colour, characterized by microcrystalline chitosan content of 7.44 wt% calculated on a polymer weight, and WRV of 1459%. The yield of product was 36 weight parts of polymer from 1000 reactor volume parts and 1 hour.

30

Example 4.

35 400 volume parts of 0.5% chitosan solution in 4% aqueous acetic acid solution characterized by properties as in Example 1 was introduced into the reactor as in Example 1. The microcrystalline chitosan dispersion was precipitated during a continuous stirring by 2.5% aqueous sodium hydroxide solution to obtain a pH

of 7.8. A 0.5% chitosan solution in 4% aqueous acetic acid solution with a constant rate of introduction of 5280 volume parts per 1 hour, and 2.5% aqueous sodium hydroxide solution with an introduction rate of 5900 volume parts per 1 hour were continuously introduced to obtain a mixture pH of 7.7 ± 0.3 . Production and purification process were the same as in Example 1.

The product was obtained in a form of stable gel with white colour, characterized by microcrystalline chitosan content of 6.5 wt% calculated on a dry polymer weight, and WRV of 1994%. The reaction yield was 26.4 weight parts of microcrystalline polymer per 1000 reactor volume parts and 1 hour.

Example 5.

400 volume parts of 0.5% chitosan solution in 2% aqueous acetic acid solution characterized by properties as in Example 1 was introduced into the reactor as in Example 1. The microcrystalline chitosan dispersion was precipitated with a continuous stirring using a 2.5% aqueous sodium hydroxide solution to obtain a mixture pH of 7.4, and a 0.5% chitosan solution in a 2% aqueous acetic acid solution was continuously introduced with the sodium hydroxide solution rate as in Example 4 to obtain a mixture pH of 7.4 ± 0.1 . Production and purification processes were the same as in Example 1. The initial microcrystalline chitosan dispersion was characterized by the value of EMP of 85 mV and after purification process the value of EMP of was 15 mV.

The product was obtained in a form of stable white gel characterized by microcrystalline chitosan content of 9.25 wt% calculated on a dry polymer weight and WRV of 850%. The product yield was 15.7 weight parts

of microcrystalline polymer per 100 reactor volume parts and 1 hour.

5 Example 6.

10 The microcrystalline chitosan dispersion was obtained in a reactor as in Example 1 using 1% chitosan solution in a 4% aqueous acetic acid solution, as well as a 7.5% aqueous sodium hydroxide solution introduced into a working circulation system. Then 1% chitosan solution in a 4% aqueous acetic acid solution with a constant introduction rate of 5280 volume parts per 1 hour, as well as a 7.5% aqueous sodium hydroxide solution with an introduction rate of 1944 volume parts per 1 hour were continuously introduced into the reaction mixture having the initial pH of 7.8, to obtain a mixture pH of 7.7 ± 0.2 . Production and purification processes were analogous to those in Example 1. The initial dispersion produced was characterized by EMP value of 99 mV and after purification the EMP was 29 mV.

25 The product was obtained in a form of stable white gel characterized by microcrystalline chitosan content of 9.05 wt%, calculated on a dry polymer weight, WRV of 587% and average molecular weight of 3.62×10^5 . The product yield was 36 weight parts of microcrystalline polymer per 1000 reactor volume parts and 1 hour.

30

Example 7.

35 500 volume parts of 0.5% chitosan solution in a 4% aqueous acetic acid solution was introduced into the reactor as in Example 1. The chitosan used was characterized by average molecular weight of 7.7×10^5 , deacetylation degree of 67.5% and WRV of 230%. The microcrystalline chitosan dispersion was precipitated

with stirring the 0.5% chitosan solution in the 4 % aqueous acetic acid to obtain a pH of 7.9, and then with a continuous method using the continuous circulation system as in Example 2. A 0.5% chitosan solution in 4% aqueous acetic acid solution with a constant introduction rate of 5280 volume parts per 1 hour, as well as 5.0% aqueous sodium hydroxide solution with a constant introduction rate of 2880 volume parts per 1 hour were introduced into the reactor, thus obtaining a mixture pH of 7.7 ± 0.3 . Production process was realized as in Example 2, whereas the purification process was realized in a ultrafiltration installation to obtain an EMP value of 9 mV.

The product was obtained in a form of stable white gel characterized by microcrystalline chitosan content of 9.05 wt%, calculated on a dry polymer weight, WRV of 830% and average molecular weight of $4.9 \cdot 10^5$. The product yield was 36 weight parts of microcrystalline polymer per 1000 reactor volume parts and 1 hour.

Example 8.

500 volume parts of 0.75 wt% chitosan solution in a 1.5 wt% aqueous acetic acid solution characterized by properties as in Example 7 was introduced into a reactor as in Example 1. The microcrystalline chitosan dispersion was precipitated with a continuous stirring using a 5.5 wt% aqueous sodium carbonate solution to obtain a mixture with a pH of 7.6, whereafter 0.75 wt% chitosan solution in a 1.5 wt% aqueous acetic acid solution was continuously introduced with constant rate of 6250 volume parts per 1. hour, and a 5.5 wt% aqueous sodium carbonate solution at a rate of 9500 volume parts per 1 hour was introduced to obtain a mixture pH of 7.6 ± 0.1 . Production and purification procedure was the same as in Example 7. The initial

microcrystalline chitosan dispersion was characterized by the value of EMP of 70 mV and after purification of the EMP was 8 mV.

- 5 The product was obtained in a form of stable white gel characterized by microcrystalline chitosan content of 4.5 wt% calculated on a dry polymer weight, and WRV of 1450%. The product yield was 19.8 weight parts of microcrystalline polymer per 1000 reactor volume parts and 1 hour.
- 10

Claims:

1. Method for continuous manufacture of microcrystal-
5 line chitosan by precipitation of chitosan from its
aqueous solutions in organic or inorganic acid, or
their salts, using aqueous solutions of alkaline
hydroxides or their salts, characterized in that
10 the chitosan solution in an aqueous acid solution,
especially in acetic acid, with polymer concentration
not lower than 0.01 wt%, preferably with polymer con-
centration within 0.1.-2.0 wt%, is continuously intro-
duced into a reactor together with an alkaline solu-
15 tion, such as an aqueous solution of an alkaline
metal hydroxide or a salt thereof having a concentra-
tion ranging from 0.1 to 20.0 wt%, whereas the chitosan
solution is introduced into the reactor with a rate
within a range of 0.1-20 volume parts per 1 hour and
20 1 reactor volume parts, and the alkaline solution is
introduced into a reactor with a rate ranging from
0.1 to 10.0 volume parts per 1 hour and 1 reactor
volume part to obtain a mixture pH of equal to or
higher than 7, whereas at the same time the microcrys-
25 talline chitosan dispersion having said pH is taken off
from the reactor by a continuous system with a rate
suitable to keep a constant reaction mixture volume
in the reactor, and the microcrystalline chitosan
dispersion is collected in a compensation tank and is
30 continuously purified, especially by continuous water
washing or by ultrafiltration method, and then the
purified microcrystalline chitosan is concentrated to
obtain a polymer content of 0.5-10.0 wt% and dried by
some well-known method.
- 35 2. A method as claimed in claim 1, characterized
in that the microcrystalline chitosan dispersion
manufactured in the reactor is subjected to continuous
circulation in a closed reactor system, whereas at

the same time a microcrystalline chitosan dispersion is carried away from the reactor by the continuous system with a rate necessary to keep a constant reaction mixture volume, and the microcrystalline chitosan dispersion is subjected to a purification process.

3. A method as claimed in the claim 2, characterized in that the alkaline solution is introduced directly to the circulation system containing the microcrystalline chitosan dispersion.

4. A method as claimed in the claims 1 and 2, characterized in that the microcrystalline chitosan purification is realized to obtain an effluent conductivity equal to the conductivity of water used.

INTERNATIONAL SEARCH REPORT

International Application No PCT/FI 90/00173

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) ⁶ According to International Patent Classification (IPC) or to both National Classification and IPC IPC5: C 08 B 37/08		
II. FIELDS SEARCHED		
Minimum Documentation Searched ⁷		
Classification System	Classification Symbols	
IPC5	C 08 B	
Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in Fields Searched ⁸		
SE,DK,FI,NO classes as above		
III. DOCUMENTS CONSIDERED TO BE RELEVANT⁹		
Category *	Citation of Document, ¹¹ with Indication, where appropriate, of the relevant passages ¹²	Relevant to Claim No. ¹³
A	Journal of Applied Polymer Science, Vol. 33, 1987 HENRYK STRUSZCZYK: "Microcrystalline Chitosan. I. Preparation and Properties of Microcrystalline Chitosan ", see page 177 - page 189 page 1 "Introduction, page 2 "Methods" --	1-4
A	Chemical Abstracts, volume 109, no. 26, 26 December 1988, (Columbus, Ohio, US), YOKOTA, HIROSHI: "Microcrystalline chitosan and manufacture ", see page 111, abstract 233068n, & Kokai Tokyo Koho 1988,, --	1-4
A	Chemical Abstracts, volume 110, no. 26, 26 June 1989, (Columbus, Ohio, US), STRUSZCZYK, H. ET AL: "Chitosan-based products, especially films, and their manufacture ", see page 105, abstract 233521a, & Valtion teknillinen Tutkimuskeskus 1988,, 28 -- -----	1-4
<div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <p>* Special categories of cited documents: ¹⁰</p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> </div> <div style="width: 45%;"> <p>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance, the claimed invention cannot be considered novel or cannot be considered to involve an inventive step</p> <p>"Y" document of particular relevance, the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.</p> <p>"&" document member of the same patent family</p> </div> </div>		
IV. CERTIFICATION		
Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report	
18th October 1990	1990 -10- 1 9	
International Searching Authority	Signature of Authorized Officer	
SWEDISH PATENT OFFICE	Sofia Nikolopoulou	

**ANNEX TO THE INTERNATIONAL SEARCH REPORT
ON INTERNATIONAL PATENT APPLICATION NO. PCT/FI 90/00173**

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report.
The members are as contained in the Swedish Patent Office EDP file on **90-09-27**
The Swedish Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent document cited in search report	Publication date	Patent family member(s)	Publication date